

1
SEQUENCE LISTING

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<120> HUMANIZED IMMUNOGLOBULIN REACTIVE WITH B7-2 AND METHODS
OF TREATMENT THEREWITH

<130> 08702.0081-00000

<140> 09/249,011

<141> 1999-02-12

<160> 24

<170> PatentIn Ver. 2.1

<210> 1

<211> 405

<212> DNA

<213> Murine sp.

<220>

<221> CDS

<222> (1)..(405)

<223> Anti-B7-2 heavy chain

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1 5 10 15

gtg cac tcc cag gtc cag ctg cag cag tct ggg cct gag ctg gtg agg 96
Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg
20 25 30

cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc gga tac aca ttc 144
Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
35 40 45

act gat tat gct ata cag tgg gtg aag cag agt cat gca aag agt cta 192
Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu
50 55 60

gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac 240
Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65 70 75 80

cag aag ttt aag ggc aag gcc aca atg act gta gac aaa tcc tcc agc 288
 Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser
 85 90 95

aca gcc tat atg gaa ctt gcc aga ttg aca tct gag gat tct gcc atc 336
 Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile
 100 105 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa gga 384
 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
 115 120 125

acc tca gtc acc gtc tcc tca 405
 Thr Ser Val Thr Val Ser Ser
 130 135

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 <213> Murine sp.

<220>
 <223> Anti-B7-2 heavy chain

<400> 2
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 Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
 35 40 45
 Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu
 50 55 60
 Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
 65 70 75 80
 Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser
 85 90 95
 Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile
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 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
 115 120 125
 Thr Ser Val Thr Val Ser Ser
 130 135

<210> 3
 <211> 396
 <212> DNA
 <213> Murine sp.

<220>
 <221> CDS
 <222> (1) .. (396)
 <223> Anti-B7-2 light chain

<400> 3
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 Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Trp Val Ser
 1 5 10 15

ggg acc tgt ggg gac att gtg ctg tca cag tct cca tcc tcc ctg gct 96
 Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
 20 25 30

gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt 144
 Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser
 35 40 45

ctg ctc aac agt aga aac cga gag aac tac ttg gct tgg tac cag cag 192
 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
 50 55 60

aaa cca ggg cag tct cct aaa ctg ctg atc tac tgg gca tcc act agg 240
 Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65 70 75 80

gaa tct ggg gtc cct gat cgc ttc aca ggc agt gga tct ggg aca gat 288
 Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
 85 90 95

ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat 336
 Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr
 100 105 110

tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag 384
 Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys
 115 120 125

ctg gaa ata aaa 396
 Leu Glu Ile Lys
 130

<210> 4
 <211> 132
 <212> PRT
 <213> Murine sp.

<220>
 <223> Anti-B7-2 light chain

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Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
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<210> 5
<211> 405
<212> DNA
<213> Artificial Sequence
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F1

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| Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly | | | | | | | | | | | | | | | | |
| 1 | | | | 5 | | | | | 10 | | | | | | 15 | |
| | | | | | | | | | | | | | | | | |
| gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag gtg aag aag | | | | | | | | | | | | | | | | 96 |
| Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys | | | | | | | | | | | | | | | | |
| | | | 20 | | | | | 25 | | | | | | 30 | | |
| | | | | | | | | | | | | | | | | |
| cct ggg agc tca gtg aag gtg tcc tgc aaa gct tcc ggc tac aca ttc | | | | | | | | | | | | | | | | 144 |
| Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe | | | | | | | | | | | | | | | | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| | | | | | | | | | | | | | | | | |
| act gat tat gct ata cag tgg gtg aga cag gct cct gga cag ggc ctc | | | | | | | | | | | | | | | | 192 |
| Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu | | | | | | | | | | | | | | | | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| | | | | | | | | | | | | | | | | |
| gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac | | | | | | | | | | | | | | | | 240 |
| Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn | | | | | | | | | | | | | | | | |
| 65 | | | | | 70 | | | | 75 | | | | | | 80 | |

cag aag ttt aag ggc aag gcc aca atg act gta gac aag tcg acg agc 288
 Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
 85 90 95

aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat acg gcc gtt 336
 Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
 100 105 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa ggt 384
 Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
 115 120 125

acc ctt gtc acc gtc tcc tca 405
 Thr Leu Val Thr Val Ser Ser
 130 135

<210> 6

<211> 135

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Humanized
 murine anti-human B7-2 heavy chain

<400> 6

Met Gly Trp Asn Cys Ile Ile Phe Phe Leu Val Thr Thr Ala Thr Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
 20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
 85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
 115 120 125

Thr Leu Val Thr Val Ser Ser
 130 135

<210> 7

<211> 396

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Humanized
murine anti-human B7-2 light chain

<220>

<221> CDS

<222> (1)..(396)

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  1          5          10          15

ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat tcc ctg gct 96
Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
          20          25          30

gta agc tta gga gag agg gcc act att agc tgc aaa tcc agt cag agt 144
Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
          35          40          45

ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag 192
Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
          50          55          60

aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca tcc act agg 240
Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
          65          70          75          80

gaa tct ggg gtc cct gat cgc ttc agt ggc agt gga tct ggg aca gat 288
Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
          85          90          95

ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg gca gtt tat 336
Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
          100          105          110

tac tgc acg caa tct tat aat ctt tac acg ttc gga cag ggg acc aag 384
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
          115          120          125

gtg gaa ata aaa 396
Val Glu Ile Lys
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<210> 8

<211> 132

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Humanized
murine anti-human B7-2 light chain

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Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu Trp Val Ser
 1 5 10 15

Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
 20 25 30

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
 35 40 45

Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
 50 55 60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
 100 105 110

Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
 115 120 125

Val Glu Ile Lys
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<210> 9

<211> 15

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR1 of
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<220>

<221> CDS

<222> (1)..(15)

<400> 9

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 Asp Tyr Ala Ile Gln
 1 5

15

<210> 10

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR1 of humanized
 murine anti-human B7-2 heavy chain

<400> 10
 Asp Tyr Ala Ile Gln
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<210> 11
 <211> 51
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: CDR2 of
 humanized murine anti-human B7-2 heavy chain

<220>
 <221> CDS
 <222> (1)..(51)

<400> 11
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 Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
 1 5 10 15

ggc 51
 Gly

<210> 12
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: CDR2 of humanized
 murine anti-human B7-2 heavy chain

<400> 12
 Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn Gln Lys Phe Lys
 1 5 10 15

Gly

<210> 13
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: CDR3 of
 humanized murine anti-human B7-2 heavy chain

<220>
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 <222> (1)..(21)

E1

<400> 13

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21

<210> 14

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR3 of humanized
murine anti-human B7-2 heavy chain

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<210> 15

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR1 of
humanized murine anti-human B7-2 light chain

<220>

<221> CDS

<222> (1)..(51)

<400> 15

aaa tcc agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg 48

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10

15

gct

Ala

51

<210> 16

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR1 of humanized
murine anti-human B7-2 light chain

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Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu

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5

10

15

Ala

<210> 17
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
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 humanized murine anti-human B7-2 light chain

<220>
 <221> CDS
 <222> (1)..(21)

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 Trp Ala Ser Thr Arg Glu Ser
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21

<210> 18
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: CDR2 of humanized
 murine anti-human B7-2 light chain

<400> 18
 Trp Ala Ser Thr Arg Glu Ser
 1 5

<210> 19
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: CDR3 of
 humanized murine anti-human B7-2 light chain

<220>
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 <222> (1)..(24)

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 Thr Gln Ser Tyr Asn Leu Tyr Thr
 1 5

24

<210> 20
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CDR3 of humanized murine anti-human B7-2 light chain

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<210> 21

<211> 1960

<212> DNA

<213> Mus sp.

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<221> CDS

<222> (12)..(408)

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<221> CDS

<222> (768)..(1087)

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Met Asp Ser Gln Ala Gln Val Leu Ile Leu Leu Leu

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10

tgg gta tct ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat 98

Trp Val Ser Gly Thr Cys Gly Asp Ile Val Leu Thr Gln Ser Pro Asp

15

20

25

tcc ctg gct gta agc tta gga gag agg gcc act att agc tgc aaa tcc 146

Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser

30

35

40

45

agt cag agt ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg 194

Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp

50

55

60

tac cag cag aaa cca ggg cag cct cct aaa ctg ctg atc tac tgg gca 242

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala

65

70

75

tcc act agg gaa tct ggg gtc cct gat cgc ttc agt ggc agt gga tct 290

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser

80

85

90

ggg aca gat ttc act ctc acc atc agc agt ctg cag gct gaa gac gtg 338

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val

95

100

105

gca gtt tat tac tgc agc caa tct tat aat ctt tac acg ttc gga cag 386

Ala Val Tyr Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln

110

115

120

125

ggg acc aag gtg gaa ata aaa c gtaagtagtc ttctcaactc tagaaattct 438

Gly Thr Lys Val Glu Ile Lys

130

三

tcaaccaaag caaatTTTTc aaaagaagaa acctgctata aagagaatca ttcattgcaa 1667
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 taagtTcatc atgggtactta gacttaatgg aatgtcatgc cttatttaca tttttaaaca 1787
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 atccacacta tactgtgaga ttaaaaacat tcattaaaat gttgcaaagg ttctataaag 1907
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<210> 22
 <211> 239
 <212> PRT
 <213> Mus sp.

<400> 22
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 20 25 30
 Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser
 35 40 45
 Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln
 50 55 60
 Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
 65 70 75 80
 Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 85 90 95
 Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
 100 105 110
 Tyr Cys Ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
 115 120 125
 Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
 130 135 140
 Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
 145 150 155 160
 Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
 165 170 175
 Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
 180 185 190
 Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
 195 200 205

E1

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
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Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 23
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 <222> (12)..(417)

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gct aca ggt gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag 98
 Ala Thr Gly Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu
 15 20 25

gtg aag aag cct ggg agc tca gtg aag gtg tcc tgc aaa gct tcc ggc 146
 Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly
 30 35 40 45

tac aca ttc act gat tat gct ata cag tgg gtg aga cag gct cct gga 194
 Tyr Thr Phe Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly
 50 55 60

cag ggc ctc gag tgg att gga gtt att aat att tac tat gat aat aca 242
 Gln Gly Leu Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr
 65 70 75

aac tac aac cag aag ttt aag ggc aag gcc aca atg act gta gac aag 290
 Asn Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys
 80 85 90

tcg acg agc aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat 338
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 95 100 105

acg gcc gtt tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg 386
 Thr Ala Val Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp
 110 115 120 125

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 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 130 135

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 Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
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 160 165 170

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 Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 175 180 185

gct gtc cta cag tcc tca gga ctc tac tcc ctc agc agc gtg gtg acc 863
 Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 190 195 200 205

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 Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
 210 215 220

cac aag ccc agc aac acc aag gtg gac aag aca gtt g gtgagaggcc 958
 His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
 225 230

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 235 240

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 Cys Pro
 245

agagtagcct gcattccaggg acaggcccca gctgggtgct gacacgtcca cctccatctc 1486

ttcctcag ca cca cct gcg gca gca ccg tca gtc ttc ctc ttc ccc cca 1535
 Ala Pro Pro Ala Ala Ala Pro Ser Val Phe Leu Phe Pro Pro
 250 255

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 Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 260 265 270 275

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 Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp
 280 285 290

tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag cca cgg gag 1679
 Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 295 300 305

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 Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val
 310 315 320

cac cag gac tgg ctg aac ggc aag gag tac aag tgc aag gtc tcc aac 1775
 His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 325 330 335

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 Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys
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 Gly Gln Pro Arg Glu Pro
 355 360

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 Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
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 Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 380 385 390

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc aca 2079
 Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 395 400 405

cct ccc atg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc 2127
 Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
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acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc 2175
 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
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gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc 2223
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
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 Leu Ser Pro Gly Lys
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Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
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Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
 85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly
 115 120 125

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 130 135 140

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
 145 150 155 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
 165 170 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 180 185 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 195 200 205
 Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 210 215 220
 Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu
 225 230 235 240
 Cys Pro Pro Cys Pro Ala Pro Pro Ala Ala Ala Pro Ser Val Phe Leu
 245 250 255
 Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
 260 265 270
 Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln
 275 280 285
 Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
 290 295 300
 Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu
 305 310 315 320
 Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
 325 330 335
 Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
 340 345 350
 Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
 355 360 365
 Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
 370 375 380
 Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
 385 390 395 400
 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly
 405 410 415
 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
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 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
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